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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,861	09/30/2005	Charles Roland Wolf	9052-229	6068

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EXAMINER	
HIRIYANNA, KELAGINAMANE T	
ART UNIT	PAPER NUMBER
1633	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,861	WOLF ET AL.	
	Examiner	Art Unit	
	Kelaginamane T. Hiriyanna	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/31/2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28,31,32 and 34* is/are pending in the application.

4a) Of the above claim(s) *31 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/05 & 11/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Restriction of invention

Applicant's election without traverse of restriction requirement in the reply filed on December 04, 2007 is acknowledged. Applicant elects with traverse the invention Group I (Claims 1-28 and 34) drawn to a method of monitoring Xenograft in a non-human animal by implanting cells that were modified before implantation for further prosecution on merits. Applicant traverses on the grounds that the examination of Group II invention, corresponding to claims 1-28 and 34 drawn to implanting cells that were modified after implantation should pose no additional burden on the examiner and further requests that the Group II be examined together with Group I inventions. Applicant is found persuasive and hence Group I and Group II inventions are hereby rejoined for the purpose of examination on the merits.

Claims 29-30, 33, 35-36 are cancelled

Claims 31-32 are withdrawn from consideration.

Applicant's election of species in the reply filed on December 04, 2007 is acknowledged.

Claims 1-28 and 34 are pending and presently under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-24 and 34 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites "genetically modifying or engineering", while the claim only implants the modified cell. It is not clear how the engineered cell is implanted. It would be remedial to make clear that the cell is "engineered" if it is modified in vivo.

Claims 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Regarding claim 11, the phrase "optionally comprises" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention.

Claims 26 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Regarding claim 26, the phrase "of protein which on death or lysis" renders the claim indefinite because it is unclear what the phrase means in the context and hence It is not clear what is being claimed. Appropriate correction is requested.

Claims 2-24 and 34 are rejected for depending from a rejected base claim(s).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-22, and 27-28 are rejected under 35 USC 102 (b) as being anticipated by Chaudhuri et al (2001, Gynecologic Oncology 83:432-438)

The above claims are drawn to a method of monitoring progression of a xenograft in a non human host animal by introducing genetically modified cell with a at least one reporter molecule or gene or agent, allowing said cell to grow and measuring a biochemical or physiological response associated with the reporter molecule or reporter gene.

Regarding claims 1-9, 13-18, 27, and 28 Chaudhuri teaches monitoring xenograft of SKOV3 cancer cell line derived cells (implanting about $4x10^6$ cells) into a nude mice, allowing for two weeks and then genetically modifying with a recombinant Adenovirus vector expressing human type-2 somatostatin receptor gene (hSSTr2) and/or Ad-GFP that act as a reporter genes and measured using a Gamma camera for detecting either the uptake of 99m-Tc-P2045 (a stomatostatin analogue) due to expression of hSSTr2 molecules and/or monitoring GFP imaging (entire article; Abstract; p.432, col.2 bridging p.433; p.435 col.1 bridging 2). Regarding claim 10 Chaudhuri teaches implanting the animal both cells that were genetically modified with (hSSTr2) and/or Ad-GFP. Regarding claim 11 and 19 Chaudhuri teaches quantitative non invasive imaging of 99m-Tc-P2045 uptake by the expressed receptor and GFP expression by measuring fluorescence (p.434, col.1, 3rd paragraph; p.435 col.1 bridging 2; Fig. 2-3). Regarding claim 12 Chaudhuri teaches that the xenografted cells expressing the reporter gene are found attached to different sites including peritoneal lining, spleen and large intestine etc (p.435, col.2 1st pragraph). Regarding claims 20-22, Chaudhuri teaches transcription control of reporter gene under a CMV promoter control (p.432, col.2, 2nd paragraph bridging p.433). The cited art thus anticipates the invention as claimed.

Claims 1-5, 7-9, 13-23, and 27-28 are rejected under 35 USC 102 (b) as being anticipated by Lin et al (2001, Int. J. Cancer 91:555-562)

The above claims are drawn to a method of monitoring progression of a xenograft in a non human host animal by introducing genetically modified cell with a at least one

reporter molecule or gene or agent, allowing said cell to grow and measuring a biochemical or physiological response associated with the reporter molecule or reporter gene.

Regarding claims 1-5, 7-9, 13-18, 27, and 28 Lin teaches monitoring xenograft of UMSCC10b head and neck carcinoma cells line derived cells that were genetically engineered and selected for expressing constructs of a reporter gene (T10b45 cells, implanted about $1x10^4$ cells at 4 sites) in a female athymic (BALB/c nu/nu) mice, (Abstract, p.555, col.2 bridging p.556). Lin further teaches regarding allowing until the tumor size reached 100 mm followed by certain treatments and then establishing a quantitative relationship between cellular injury and EGF expression (p.559, col.1) in vivo. Regarding claim 11 and 19 Lin teaches quantitative measurements of relationship between cellular injury and EGFP expression by measuring in cisplatin treated and untreated tumor cells (p.559, col.1 bridging col.2; Fig.6). Regarding claims 20-23, Lin teaches transcription control of reporter gene under a GADD153 promoter control (Abstract; p.555, col.2, 3rd paragraph bridging p.556; Fig.1). The cited art thus anticipates the invention as claimed.

Claims 1-5, 7-9, 13-22, 24-25, 27-28 and 34 are rejected under 35 USC 102 (e) as being anticipated by Vogelstein et al (Patent No: US 6926,890 B2)

The above claims are drawn to a method of monitoring progression of a xenograft in a non human host animal by introducing genetically modified cell with a at least one reporter molecule or gene or agent, allowing said cell to grow and measuring a biochemical or physiological response associated with the reporter molecule or reporter gene.

Regarding claims 1-5, 7-9, 13-18, 27, and 28 Vogelstein teaches monitoring xenograft of SW480 human colon carcinoma cells line derived cells that were genetically engineered and selected for expressing constructs of a reporter gene Beta-hCG (SW480 CG cell line implanted about $3x10^6$ cells by subcutaneous injection) in a female athymic (nu/nu) mice and placed them for at least 3 hrs before measurements (Abstract; col.8,

lines 35-38; col.8, lines 45-59). Regarding claim 11 and 19 Vogelstein teaches quantitative measurements of relationship between tumor burdens and urinary beta-hCG levels or other reporters (col.5 , lines 35-68; col.10, lines col. 9-10; col.4, lines 12-27). Regarding claims 20-22, Vogelstein teaches transcription control of reporter gene under a viral or metallothionein promoter etc., control (col.4, lines 51-65). Regarding claim 24-25 and 34 Vogelstein teaches a post-transcriptional reporting mediated by reported excreted in urine and testing the effects therapeutic agents on various tumors (Abstract; col.10, lines col. 9-10; col.3, lines 1-40; col.6 lines 57-67 bridging col.7). The cited art thus anticipates the invention as claimed.

Claims 1-5, 7-9, 13-22, and 24-28 and 34 are rejected under 35 USC 102 (e) as being anticipated by Risau et al (WO 98/56936).

The above claims are drawn to a method of monitoring progression of a xenograft in a non human host animal by introducing genetically modified cell with a at least one reporter molecule or gene or agent, allowing said cell to grow and measuring a biochemical or physiological response associated with the reporter molecule or reporter gene.

Regarding claims 1-5, 7-9, 13-18, 27, and 28 Risau teaches monitoring xenograft of GS9L glioma cells that were genetically engineered and selected for expressing hpoxia-inducible constructs of a reporter gene Beta-galactosidase, wherein it is regulated by a 3'mRNA stabilization element of VEGF and further comprises a nuclear localization signal (p.32, example 1 and p.33 example 2). The above cell line was implanted by subcutaneous injection in a syngenic Fischer rat and the tumor developed was analyzed excising and detecting beta-galactosidase activity (p.33, 3rd paragraph bridging p.34 2nd paragraph). Regarding claim 11 and 19 Risau teaches quantitative measurements of relationship between tumor and the hypoxia inducible reporter gene expression expression in tumors (p.35-36). Regarding claims 20-22, Risau teaches transcription control of reporter gene under a SV40 promoter (p.33, 2nd pargraph). Regarding claim 24-26 and 34 Risau teaches a post-transcriptional reporting mediated by reporter proteins

or therapeutic proteins including HIF, apoptosis proteins, proteases, growth factors, p53 etc or antisense RNAs ((p.12 2nd paragraph bridging p.13-14). The cited art thus anticipates the invention as claimed.

Conclusion:

No claim allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanna Ph.D.,* whose telephone number is (571) 272-3307. The examiner can normally be reached Monday through Friday from 9 AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Joseph Woitach Ph.D.*, may be reached at (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

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